October 1, 2002

C. Tucker Helmes, Ph.D.
ETAD North America Disperse Blue 79:1 Coalition
1850 M Street, NW
Suite 700
Washington, DC 20036

Dear Dr. Helmes:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Disperse Blue 79:1, posted on the ChemRTK HPV Challenge Program Web site on February 20, 2002. I commend the ETAD North America Disperse Blue 79:1 consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the ETAD North America Disperse Blue 79:1 consortium advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
N-[5-[bis[2-(Acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-methoxyphenyl]acetamide

SUMMARY OF EPA COMMENTS

The sponsor, the ETAD North America Disperse Blue 79:1 Consortium, submitted a test plan and robust summaries to EPA on January 7, 2002, for N-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-methoxyphenyl]acetamide (C.I. Disperse Blue 79:1, CAS No. 3618-72-2). EPA posted the submission on the Chemical RTK HPV Challenge Web site on February 20, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The submitter needs to provide level III fugacity data for this chemical.

2. Health Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program. However, the submitter needs to clarify certain information in the test plan and add details to some of the robust summaries. The submitter also needs to provide a separate robust summary for the reproductive toxicity endpoint using data from the repeated-dose and developmental toxicity studies.

3. Ecological Effects. Adequate vertebrate chronic test data are available to fulfill the SIDS-level endpoints for the purposes of the HPV Challenge Program. Aquatic acute testing is not necessary owing to the chemical's very low water solubility. The submitted acute data were judged inadequate for the reasons given below.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE N-[5-[BIS[2-(ACETYLOXY)ETHYL]AMINO]-2-[(2-BROMO-4,6-DINITROPHENYL)AZO]-4-METHOXYPHENYL]ACETAMIDE CHALLENGE SUBMISSION

Test Plan

EPA agrees with the submitter's proposal to use data for the analog C.I. Disperse Blue 79 to address some SIDS endpoints for C.I. Disperse Blue 79:1 for the purposes of the HPV Challenge Program, given the similarity in chemical structure and properties between the two chemicals. However, the submitter needs to indicate clearly in both the text and Table 1 of the test plan which data are taken from the analog studies.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)

The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data presented for photodegradation are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The data presented by the submitter are not adequate to address this endpoint because they are not from ready biodegradability tests. However, ready biodegradation data for chemical analogs

lead EPA to consider this chemical to be not readily biodegradable

Stability in water. The submitter did not provide information relevant to the hydrolysis of this chemical. The only study provided addressed a biotic reduction in sediment. However, because the solubility of disperse blue 79:1 is very low (0.0052 mg/L) and the acetylaniline function has little potential for hydrolysis under environmental conditions, it is not necessary to test this substance for hydrolysis using OECD Guideline 111 (which applies only to water-soluble compounds).

Fugacity. The submitter reports that because of the large K_{ow} and low water solubility, disperse blue 79:1 has the potential to bioconcentrate in aquatic organisms and will adsorb to sediment and suspended solids in the water column. This intuitive analysis is inadequate and the submitter needs to use a level III fugacity model to predict the partitioning behavior of the compound.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The data are adequate for all endpoints for the purposes of the HPV Challenge Program.

The NOAELs presented in Table 1 of the test plan should be expressed as "=" rather than ">". If the NOAEL is the highest dose in the study, the submitter should use the following notation: "= X mg/kg/day (highest dose tested)."

Acute toxicity. Although the submitted acute range-finding study was not a standard acute toxicity test, the data allow for an adequate characterization of the acute toxicity of the substance.

Reproductive/developmental toxicity. A reproductive toxicity study is not available. EPA considers that adequate documentation of the histopathological evaluation of reproductive organs in the repeated-dose toxicity study and the available adequate developmental toxicity study address these endpoints for the purposes of the HPV Challenge Program.

In Table 1, the NOAELs for reproductive toxicity are listed as > 2000 mg/kg for rats and > 100 mg/kg for rabbits. However, these values refer to the maternal toxicity NOAELs from the developmental toxicity studies and they do not necessarily reflect reproductive toxicity. Specifically, the rabbit NOAEL is based on changes in maternal body weight. Also, reproductive toxicity NOAELs derived from repeated-dose studies that evaluated the histopathology of reproductive organs need to be included.

Ecological Effects (fish, invertebrate and algal toxicity)

Adequate data on C.I. Disperse Blue 79:1 are available for these endpoints. Although the submitted analog acute aquatic test data are not adequate, chronic data are preferable in this case because no acute effects are expected at the chemical's aqueous solubility limit. The available chronic fish data on C.I. Disperse Blue 79:1 may be used in lieu of an invertebrate (daphnid) reproduction test for the purposes of the HPV Challenge Program.

Fish. An early life stage chronic toxicity study on C.I. Disperse Blue 79:1, performed pursuant to a 1989 EPA Enforceable Consent Order (54 FR 48012), was submitted for this endpoint.

Invertebrates and algae. The submitted analog acute test data are not reliable because endpoints were tested above the chemical's aqueous water solubility, test durations were inadequate, and chemical purity was not characterized.

Specific Comments on Robust Summaries

Health Effects

Repeated-dose toxicity. Information missing from the robust summary includes the number of animals per dose group and the statistical methods used to evaluate the results. The NOAEL should be expressed as "= 2500 mg/kg/day (highest dose tested)."

Genotoxicity (gene mutations). In the Ames study on "Foron Navy SE-2GRL" the following information was not provided: GLP status, identity of the test substance and whether it is an analog, purity of the test substance, whether the positive results were seen with or without activation, and the reason for limiting the upper dose to 1000 ：g/plate.

Genotoxicity (chromosomal aberrations). The submitter needs to add study details to the micronucleus test robust summary in accordance with HPV guidance for preparing robust summaries at http://www.epa.gov/opptintr/chemrtk/robsumgd.htm.

Reproductive toxicity. There was no robust summary for this endpoint. A robust summary should be prepared from the information in the repeated-dose and developmental toxicity studies. The robust summary should specify whether reproductive organs were examined macroscopically and microscopically and should include the results of these evaluations. The robust summary should also discuss methods and results used to assess other reproductive outcomes.

Developmental toxicity. The description of "Methods" needs to be expanded for both studies and information on the number/litter examined for external, visceral, or skeletal malformations should be reported. Statistical and analytical methods need to be included, and the biological significance of maternal gestational weight changes and "slight reductions" in fetal weight changes needs to be clearly explained. (Note: EPA evaluations conducted in 1992 identified the following values from results of the two submitted studies: (a) for the rat study, a maternal LOAEL of 500 mg/kg/day based on clinical signs (including alopecia, piloerection, and dark feces); (b) for the rabbit study, a maternal NOAEL of 300 mg/kg based on reduced body weight gain and a developmental NOAEL of 600 mg/kg based on no evidence of toxicity (U.S. EPA, 1993).)

Ecotoxicity

Fish. A missing critical data element is dissolved oxygen content.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

Reference

U.S. EPA. 1993. Letter with attachments from C. Auer, U.S. Environmental Protection Agency to Dr. T. Helmes, Ecological and Toxicological Association of the Dyestuffs Manufacturing Industry. January 11. EPA OPPT Docket AR085-006.

(Administrative Record (AR) materials are available for public viewing at the EPA Docket Center, Rm. B102-Reading Room, EPA West, 1301 Constitution Ave., NW., Washington, DC. The EPA Docket Center is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the OPPT Docket, located in the EPA Docket Center, is (202) 566-0280.)